factors. The main claim relates to the isolated, stabilized ß-catenin and its fragments, yet such fragments were not indicated.

On the one hand the invention described here is aimed at making available new agents for treating cancers or aberrant tissue and organ developments. It is based on the special task to affect the interaction between ß-catenin and LEF/TCF transcription factors as a prerequisite to the translocation and activity of the complex in the cell nucleus. This modulation shall be specific, i.e. it shall not interfere with other interactions of ß-catenin (e.g. with APC, conductin or E-cadherin). In addition, the invention is aimed at developing ELISA methods for screening substance libraries to detect molecules (a. o. peptides, organic compounds) which highly specifically affect always only one interaction of ß-catenin.

The invention is implemented according to the claims, the sub-claims are preferential variants.

In a first implementation of the invention the binding domains of the LEF/TCF transcription factors for ß-catenin were identified (Fig. 1). They are the starting point for obtaining peptides and similar molecules according to the invention. These peptides consist preferably of sequences containing 10-20 amino acids from the N-terminal domain of LEF-1 or TCF-4 (Fig. 2). These are especially preferably peptides

- consisting of the N-terminal amino acids 11-34 of LEF-1 (Fig. 1) with the following sequence
  substitute → GDPELCATDEMIPFKDEGDPQKEK (SEQ ID NO: 1)

- substitute → consisting of the N-terminal amino acids 14-27 of LEF-1 with the following sequence
  ELCATDEMIPFKDE (SEQ ID NO: 2)

- substitute → consisting of the the N-terminal amino acids 7-29 (Fig. 2) with the following sequence
  GGDDLGANDELISFKDEGEQEEK (SEQ ID NO: 3)

- substitute → consisting of the N-terminal amino acids 10-23 of TCF-4 with the following sequence
  DLGANDELISFKDE (SEQ ID NO: 4)

Furthermore, peptides where acid amino acids are arranged at a distance of 5 amino acids and flanked by hydrophobic and basic amino acids are preferred (Fig. 2).

These peptides may be used for treating tumors according to the invention with two principle ways being possible.

a) Use of peptides as such

A direct use of peptides for treating tumors is, in general, out of question owing to their instability towards proteases and owing to the lack of membrane permeability. Stabilizing is effected by coupling with a second peptide, for which the so-called antennapedia peptide RQIEIWFQNRRMEWEE is excellently suited. This peptide is in a position to transport up to 100 amino acid long, coupled peptides through cell membranes into the cytoplasma and the cell nucleus. The coupled peptides may be used in treating tumors in a favourable way.

b) Use of peptides for drug design (peptide mimikry)

The peptides according to the invention serve also as a basis for designing substances which increase the stability and efficiency in the cell by a purposeful modification (peptidomimetics). This may be e.g. reached by adding reactive groups, substituting amino acids or design of non-hydrolizable peptide-like bonds.

By substituting the carbon skeleton of the peptides by synthetic carbon skeletons with the same arrangement of functional groups the stability of the molecules may be also increased (non-peptidomimetics). This molecular mimikry of the biological activity of inhibitory peptides derived from the minimum binding domain of LEF-1/TCF for ß-catenin (Figs. 3 and 4) allows the production of more potent agents for treating tumors.

In a second step to implement the invention the regions of ß-catenin which are responsible for the specific bonds with LEF-1/TCF-4, APC domains (containing 20 and 15 amino acid repeats), conductin and E-cadherin were identified. It was detected that these regions overlap partly and concern the armadillo domains 3-8 of ß-catenin (Figs 5 and 6). The central point of this surprising finding is that mutations of ß-catenin were produced which prevent specific

Tab.1

Aminosäuresequenz des humanen β-Catenin (Armadillo-Repeats 3-9)

arm	3	(224-264)	HREGLLAIFKSGGIPALVKMLGSPVDSVLFYAITTLHNLLL	(SEQ ID NO:6)
arm	4	(265-306)	HQEGA MAVRLAGGLQKMVALLNKTNVKFLAITTDCLQILAY	(SEQ ID NO:7)
arm	5	(307-349)	GNQESKLIILASGGPQALVNIMRTYTYEKLLWTTSRVLKVLSV	(SEQ ID NO:8)
arm	6	(350-390)	CSSNKPAIVEAGGMQALGLHLTDPSQRLVQNCLWTLRNLSD	(SEQ ID NO:9)
arm	7	(391-429)	AATKQEGMEGLLGTLVQLLGSDDINVVTCAAGILSNLTC	(SEQ ID NO:10)
arm	8	(430-473)	NNYKNKMMVCQVGGIEALVRTVLRAGDREDITEPAICALRHLTS	(SEQ ID NO:11)
arm	9	(474-519)	RHQEAEMAQNAVRLHYGLPVVVKLLHPPSHWPLIKATVGLIRNLAL	(SEQ ID NO:12)

Substitute